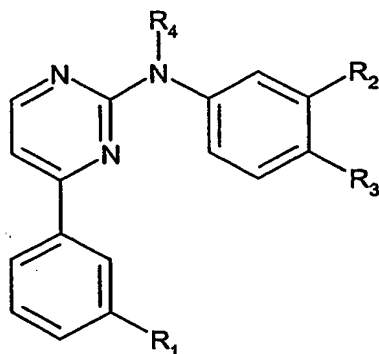


Patent Claims

1. A compound of formula



5 wherein

R_1 is halogen or halo(C_{1-4})alkyl,

R_2 is hydrogen, halogen or halo(C_{1-4})alkyl,

R_3 is halogen or halo(C_{1-4})alkyl,

R_4 is hydrogen, (C_{1-8})alkyl, hydroxy(C_{1-6})alkyl or a group of formula

10 -CO- R_5 ,

-CO-(CH_2) $_m$ -OR $_6$,

-CO-CO- R_7 ,

-CO-CO-OR $_8$,

-CO-N(R_9R_{10}),

15 -CO-(CH_2) $_n$ -CO- R_{11} ,

-CO-(CHR $_{15}$)-O-(CH_2) $_o$ -CO- R_{11} ,

-CO-(CH_2) $_p$ -O-(CH_2) $_q$ -O-(CH_2) $_r$ - R_{16} ,

-CO-O-(CH_2) $_s$ -O-CO- R_{17} ,

-CO-O-(CH_2) $_t$ -N($R_{18}R_{19}$),

20 -CO-O-(CH_2) $_u$ -NH-CO-CH(NH $_2$)- R_{20} , or

-CO-O-(CH_2) $_w$ -NH-CO- R_{17} , wherein

R_5 is hydrogen, (C_{1-8})alkyl, (C_{3-8})cycloalkyl, amino, (C_{1-4})alkylamino,

di(C_{1-4})alkylamino, aryl or heterocyclyl which is a 5 or 6-membered heterocyclic ring system having 1 to 4 heteroatoms selected from N, O or S,

25 R_6 is hydrogen, (C_{1-4})alkyl, (C_{3-8})cycloalkyl, aryl, (C_{1-4})alkyl substituted by

heterocyclyl which is a 5 or 6-membered heterocyclic ring system having 1 to 4 heteroatoms selected from N, O or S, amino(C_{1-6})alkyl,

(C_{1-4})alkylamino(C_{1-6})alkyl, di(C_{1-4})alkylamino(C_{1-6})alkyl, hydroxy(C_{1-6})alkyl,

hydroxy(C_{1-4})alkylamino(C_{1-6})alkyl or an amino acid residue,

e.g. $-\text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH}$,

R_7 and R_8 independently of each other are (C_{1-4}) alkyl, (C_{3-8}) cycloalkyl, aryl or heterocyclyl which is a 5 or 6-membered heterocyclic ring system having 1 to 4 heteroatoms selected from N, O or S,

R_9 and R_{10} independently of each other are hydrogen or (C_{1-4}) alkyl or one of R_9 and R_{10} is hydrogen and the other is (C_{3-8}) cycloalkyl, (C_{1-4}) alkyl, aryl or heterocyclyl,

R_{11} is (C_{1-4}) alkyl, $-\text{OR}_{12}$, $-\text{NR}_{13}\text{R}_{14}$, an amino acid, an (C_{1-4}) alkylester thereof or a di (C_{1-4}) alkylester thereof,

R_{12} is hydrogen or (C_{1-4}) alkyl,

R_{13} and R_{14} independently of each other are hydrogen, (C_{1-4}) alkyl, amino (C_{1-6}) alkyl, (C_{1-4}) alkylamino (C_{1-6}) alkyl, di (C_{1-4}) alkylamino (C_{1-6}) alkyl,

R_{15} is hydrogen or (C_{1-4}) alkyl,

R_{16} is hydrogen, (C_{1-4}) alkyl, carboxyl or carboxylic ester,

R_{17} is amino (C_{1-4}) alkyl, (C_{1-4}) alkylamino (C_{1-4}) alkyl or di (C_{1-4}) alkylamino (C_{1-4}) alkyl,

R_{18} is hydrogen or (C_{1-4}) alkyl,

R_{19} is hydroxy (C_{1-4}) alkyl,

R_{20} is (C_{1-4}) alkyl or hydroxy (C_{1-4}) alkyl,

m is 0 to 4,

n is 2 to 8,

o is 0 to 4,

p is 0 to 4,

q is 1 to 8,

r is 0 to 4,

s is 1 to 4,

t is 1 to 4,

u is 1 to 6 and

w is 1 to 6.

2. A compound of claim 1 wherein

- R_1 is chloro or trifluoromethyl,

- R_2 is hydrogen or trifluoromethyl,

- R_3 is chloro, fluoro or trifluoromethyl,

- R_4 is hydrogen, (C_{1-4}) alkyl, e.g. methyl, hydroxy (C_{1-4}) alkyl, e.g. hydroxyethyl, or a group of

formula

$-\text{CO}-\text{R}_5$,

-CO-(CH₂)_m-OR₆,

-CO-CO-R₇,

-CO-CO-OR₈,

-CO-N(R₉R₁₀),

-CO-(CH₂)_n-CO-R₁₁,

-CO-(CHR₁₅)-O-(CH₂)_o-CO-R₁₁,

-CO-(CH₂)_p-O-(CH₂)_q-O-(CH₂)_r-R₁₆,

-CO-O-(CH₂)_s-O-CO-R₁₇,

-CO-O-(CH₂)_t-N(R₁₈R₁₉),

-CO-O-(CH₂)_u-NH-CO-CH(NH₂)-R₂₀, or

-CO-O-(CH₂)_w-NH-CO-R₁₇, wherein

R₅ is hydrogen, (C₁₋₄)alkyl, (C₃₋₆)cycloalkyl, dimethylamino, phenyl or heterocyclyl which is a 6-membered heterocyclic ring system having one O as a heteroatom, e.g. tetrahydropyranyl,

R₆ is hydrogen, (C₁₋₄)alkyl, (C₁₋₂)alkyl substituted by heterocyclyl which is a 5 or 6-membered heterocyclic ring system having 1 or 2 heteroatoms selected from N or O, e.g. including unsubstituted pyrrolidine, morpholine and piperazine and piperazine substituted by e.g. (C₁₋₂)alkyl or (C₁₋₂)hydroxyalkyl;

amino(C₁₋₄)alkyl, (C₁₋₂)alkylamino(C₁₋₄)alkyl, di(C₁₋₂)alkylamino(C₁₋₄)alkyl, hydroxy(C₁₋₃)alkyl, hydroxy(C₁₋₂)alkylamino(C₁₋₂)alkyl or an amino acid residue, e.g. -CH₂-CH(NH₂)-COOH,

R₇ and R₈ independently of each other are (C₁₋₂)alkyl or phenyl,

R₉ and R₁₀ independently of each other are hydrogen or (C₁₋₂)alkyl,

R₁₁ is (C₁₋₂)alkyl, -OR₁₂, -NR₁₃R₁₄, an amino acid, an (C₁₋₂)alkylester thereof or an di(C₁₋₂)alkylester thereof, preferably an amino acid selected from the group consisting of alanine, phenylalanine, glutamic acid and lysine, wherein the binding is effected via the α-amino group or in the case of e.g. lysine via the ε-amino group,

R₁₂ is hydrogen or (C₁₋₂)alkyl,

R₁₃ and R₁₄ independently of each other are hydrogen, (C₁₋₂)alkyl,

amino(C₁₋₄)alkyl, (C₁₋₂)alkylamino(C₁₋₄)alkyl, di(C₁₋₂)alkylamino(C₁₋₄)alkyl,

R₁₅ is hydrogen or (C₁₋₂)alkyl,

R₁₆ is hydrogen, (C₁₋₂)alkyl, carboxyl or carboxylic ester,

R₁₇ is amino(C₁₋₂)alkyl,

R₁₈ is hydrogen or (C₁₋₂)alkyl,

R₁₉ is hydroxy(C₁₋₂)alkyl,

R_{20} is (C_{1-2}) alkyl or hydroxy (C_{1-2}) alkyl,

m is 0 or 1,

n is 2 to 4,

o is 0 or 1,

p is 0 to 2,

q is 2 to 5,

r is 0 to 2,

s is 2,

t is 2,

u is 1 to 3 and

w is 1 to 3.

3. A compound according to claim 1 or 2 which is a compound of formula I wherein

R_1 is chloro,

R_2 is hydrogen,

R_3 is trifluoromethyl and

R_4 is hydrogen.

4. A compound according to claim 1 or 2 which is a compound of formula I wherein

R_1 is chloro,

R_2 is hydrogen,

R_3 is trifluoromethyl and

R_4 is a group of formula $-\text{CO}-\text{O}-(\text{CH}_2)_2-\text{N}[(\text{C}_2\text{H}_5\text{OH})(\text{CH}_3)]$.

5. A compound according to any one of claims 1 to 4 in the form of a salt.

6. Use of a compound of any one of claims 1 to 5 in the preparation of a medicament for the therapy of IgE-synthesis-mediated diseases, autoimmune diseases, gastrointestinal diseases and chronic rejection of transplants.

7. A method of treatment of IgE-synthesis-mediated diseases, autoimmune diseases, gastrointestinal diseases and chronic rejection of transplants which method comprises administering a therapeutically effective amount of a compound of any one of claims 1 to 5 to a subject in need of such treatment.

8. A compound of any one of claims 1 to 5 for use as a pharmaceutical.

9. A pharmaceutical composition comprising a compound of any one of claims 1 to 5 in association with at least one pharmaceutical excipient.
- 5 10. Use of an amine, which is substituted by
- phenyl-substituted pyrimidin; and
 - phenyl; and
 - a third substituent, e.g. R_4 as defined in claim 1 to 5,
- 10 in the preparation of a medicament for the treatment of IgE-synthesis-mediated diseases, autoimmune diseases, gastrointestinal diseases and chronic rejection of transplants.